Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Initially, applicants would like to point out that the admission contained within the November 7, 2003, submission is limited to nucleic acids encoding hypersensitive response elicitors from *bacterial* pathogen, which hypersensitive response elicitors, as demonstrated by the previously submitted Declaration of Zhong Min Wei Under 37 C.F.R. § 1.132 as well as the (Second) Declaration of Zhong Min Wei Under 37 C.F.R. § 1.132 (enclosed herewith) ("Second Wei Declaration"), belong to an art-recognized class of proteins. No such admission was made with respect to other hypersensitive response elicitor proteins or polypeptides of *Phytophthora*, such as elicitins.

Claims 48, 54, 68, 74, 78, and 79 have been canceled without prejudice; claims 41, 42, 53, 59, 61, 62, 75, and 76 have been amended; and new claims 80-85 have been introduced.

The objection to claims 48, 54, 68, and 74 is rendered moot by the cancellation of these claims without prejudice.

The rejection of claims 41-44, 49-53, 58-64, 69-73 and 75-77 under 35 U.S.C. § 112, first paragraph, as lacking written descriptive support for the claimed genus is respectfully traversed.

The burden of establishing that an application lacks adequate written descriptive support falls on the PTO. *See In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976) ("[T]he PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims."). Hence, the PTO must demonstrate *why* the disclosure is insufficient.

The PTO has taken the position at pages 4-6 of the outstanding office action that the four exemplary nucleic acids (SEQ ID NO: 2 encoding HrpN of *Erwinia chrysanthemi*, SEQ ID NO: 4 encoding HrpN of *Erwinia amylovora*, SEQ ID NO: 6 encoding HrpZ of *Pseudomonas syringae*, and SEQ ID NO: 8 encoding PopA1 of *Pseudomonas solanacearum*) are not representative of the claimed genus. The basis for the

PTO's position is that a number of pathogen species—in the sense of biological classification—exist, and hypersensitive response elicitors from only several of the many pathogen species have been described in the specification. Applicants submit that this basis for asserting lack of written descriptive support is insufficient.

The Federal Circuit has clearly espoused that *per se* conclusions of written description violations cannot be founded upon the basis of genus size alone. *See Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1326-27, 63 USPQ2d 1609, 1614-15 (Fed. Cir. 2002) (refusing to adopt position that three species as a matter of law cannot satisfy written description requirement for significantly larger genus). Thus, the PTO's conclusion cannot be based on genus size alone. But that is precisely what the PTO has done at pages 4-6 of the outstanding office action. The PTO lists numerous organisms, suggests that the majority of these organisms would produce at least one hypersensitive response elicitor, and then concludes that neither the claimed genus nor the subgenera from any bacteria are adequately described. Because the PTO's position is unsupported by law and unsupported by any facts other than genus size, applicants submit that the PTO's position cannot be sustained.

With respect to the PTO's citation of several hypersensitive response elicitors identified after the priority filing date of the present application (e.g., HrpW of *Erwinia amylovora* and *Pseudomonas syringae*), it should be noted that the specification teaches those of skill in the art that these elicitors, too, can be used to practice the invention even though their nucleotide and amino acid sequences are not recited specifically in the specification. It should be noted that the "Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶ 1, 'Written Description' Requirement," make explicitly clear that the description of a representative number of species does *not* require the description to be of such a nature that it would provide support for each species that the genus embraces. 66 Fed. Reg. 1099, 1106 (2001). Hence, the absence of sequences for the later-identified HrpW elicitors is irrelevant to the issue of whether the present specification provides adequate written descriptive support for their use in accordance with the present invention.

Moreover, the conclusion by the PTO is contrary to evidence submitted herewith by applicants. As demonstrated by the accompanying Second Wei Declaration, one of ordinary skill in the art would have understood that applicants were in possession of the presently claimed invention at the time the present application was filed. This is so, because the four exemplary species were recognized at the time of filing as belonging to an art-

recognized class of hypersensitive response eliciting proteins produced by bacterial plant pathogens.

One reason why the disclosed species are representative of the claimed genus is because the species were recognized as structurally and functionally conserved. For example, it was known that hypersensitive response elicitors within a given genus—again, in the sense of biological classification—are often homologous to elicitors from different pathogenic species and strains of the same genus. *See* Second Wei Declaration ¶ 6. This has been demonstrated among HrpN homologs from *Erwinia*, where the *Erwinia amylovora hrpN* gene has been used to clone other *hrpN* homologs from different *Erwinia* species (*see* Second Wei Declaration ¶¶ 7-10); and HrpZ homologs from *Pseudomonas*, where the *Pseudomonas syringae hrpZ* gene has been used to clone other *hrpZ* homologs from different *Pseudomonas syringae* pathovars (*see* Second Wei Declaration ¶ 11). Thus, one of ordinary skill in the art would expect structural conservation of hypersensitive response elicitors, at least among the pathogens classified as belonging to the same genus (again, in the sense of biological classification).

Another reason why the disclosed species are representative of the claimed genus is because the encoding genes are similarly regulated, expressed, and secreted by their source organisms. For instance, the genes encoding hypersensitive response elicitors are positioned within the *hrp* gene cluster or proximate to the *hrp* gene cluster in *hrp* regulons. *See* Second Wei Declaration ¶ 12. Substantially all hypersensitive response elicitors identified have been shown to be secreted through the type III (or *hrp*-dependent) secretion pathway, which is a highly conserved and unique mechanism for the delivery of pathogenicity related molecules in gram-negative bacteria. *See* Second Wei Declaration ¶ 14. Finally, expression of the genes encoding the *hrp* gene cluster is induced under conditions that mimic the plant apoplast, such as low concentrations of carbon and nitrogen, low temperature, and low pH. *See* Second Wei Declaration ¶ 15. Thus, because the encoding genes are similarly regulated, expressed, and secreted by their source organisms, one of ordinary skill in the art would expect other hypersensitive response elicitor genes to behave similarly.

Another reason why the disclosed species are representative of the claimed genus is because the disclosed species are characterized by a number of common biochemical characteristics which were known to those of skill in the art prior to the filing date of the

present application. These include being glycine rich, heat stable, hydrophilic, lacking of an N-terminal signal sequence, and susceptible to proteolysis. *See* Second Wei Declaration ¶ 16.

A final reason why the disclosed species are representative of the claimed genus is because these species share the ability to induce specific plant responses. The induction of plant disease resistance, plant growth enhancement, and plant stress resistance are three plant responses that result from treatment of plants or plant seeds with a hypersensitive response elicitor from a bacterial plant pathogen. *See* Second Wei Declaration ¶ 18. With respect to disease resistance, topical application of HrpN from *Erwinia amylovora* resulted in disease resistance to plants for a broad range of plant pathogens (*see* Second Wei Declaration ¶ 19), topical application of HrpZ from *Pseudomonas syringae* resulted in disease resistance to plants for a diverse range of plant pathogens (*see* Second Wei Declaration ¶ 20), and topical application of HreX from *Xanthomonas campestris* resulted in disease resistance to plants for a range of plant pathogens (*see* Second Wei Declaration ¶¶ 22-24). This ability to induce disease resistance via topical application also has been borne-out via transgenic expression. For example, constitutive transgenic expression of HrpZ from *Pseudomonas syringae* resulted in disease resistance to plants for a several plant pathogens (*see* Second Wei Declaration ¶ 21), and constitutive transgenic expression of HrpN from *Erwinia amylovora* likewise resulted in disease resistance to plants for several plant pathogens (*see* Second Wei Declaration ¶¶ 28-30). Because disease resistance has been demonstrated for topical application of HrpN of *Erwinia amylovora*, HrpZ of *Pseudomonas syringae*, and HreX of *Xanthomonas campestris*, and transgenic expression of *hrpN* of *Erwinia amylovora* and *hrpZ* of *Pseudomonas syringae*, one of ordinary skill in the art would expect other members of this art-recognized class to likewise induce disease resistance in plants following topical application or transgenic expression thereof (*see* Second Wei Declaration ¶ 31).

Thus, applicants have presented a body of evidence demonstrating that the four species belong to an art-recognized class of proteins from bacterial plant pathogens; that structural conservation exists among homologs of the different hypersensitive response elicitor proteins; that hypersensitive response elicitor genes are similarly regulated, expressed, and secreted by type III secretion systems of their source organisms; that the hypersensitive response elicitor proteins are characterized by a number of common biochemical characteristics which were known to those of skill in the art prior to the filing date of the present application; and that the hypersensitive response elicitor proteins of this

art-recognized class are functionally similar in their ability to induce similar plant responses, particularly systemic acquired resistance against plant pathogens that cause disease. The PTO, on the other hand, has merely suggested that the genus is large and may contain many species—though the PTO did not demonstrate that the genus contains structurally and functionally unrelated species.

For all these reasons, the rejection of claims 41-44, 49-53, 58-64, 69-73 and 75-77 as lacking written descriptive support and should be withdrawn.

The rejection of claims 41-54 and 58-79 under 35 U.S.C. § 112, first paragraph, for lack of enablement is respectfully traversed.

The rejection is premised on the asserted failure to teach one of ordinary skill in the art how to make and/or use the invention with regard to species of nucleic acids (encoding hypersensitive response elicitors) that are not described by nucleotide sequence in the present application. For substantially the same reasons noted above, applicants submit that this rejection is improper.

All that is needed is objective enablement of what is claimed. *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). That is precisely what the specification provides, when the disclosure is considered with the state of the art at the time the application was filed. One of ordinary skill in the art is fully capable of identifying other hypersensitive response elicitor-encoding nucleic acids (*see* Second Wei Declaration ¶¶ 6-11), determining whether the encoded protein does, in fact, induce a hypersensitive response in non-host plants (*see* Second Wei Declaration ¶ 5), preparing DNA constructs and transforming plants as described in the specification at page 36, lines 6-30, and then ascertaining whether the transformed plants are in fact disease resistant (*see* Examples 1-8; *see also* Second Wei Declaration ¶¶ 21 and 28-30 (describing methods of testing for disease resistance)). Thus, the teachings of the present application, coupled with the knowledge in the art, would have allowed one of skill in the art to practice the claimed invention within the full scope of the claims, even with nucleic acids not explicitly disclosed therein.

The PTO has suggested that seed propagation would not have been used for a number of plants that are normally propagated via cuttings. The PTO's position may be correct with respect to commercial varieties of these plants, but is clearly incorrect with respect to varieties of these plants that breeders use to establish new commercial varieties (i.e., by traditional plant breeding techniques). Hence, the PTO's position fails in this regard. Moreover, the mere fact that one of skill in the art may not choose to practice the present

invention in a particular plant species (i.e., for commercial reasons) is irrelevant to whether the claimed invention is enabled. That is, the position of the PTO is not that the claimed invention will not operate in those plants traditionally propagated by cuttings, but that it would not be commercially practical to do so. That does not negate objective enablement of the present invention.

For these reasons, the rejection of claims 41-54 and 58-79 for lack of enablement is improper and should be withdrawn.

The rejection of claims 42-48, 52, 53, 59, 61-74, 76, and 79 under 35 U.S.C. § 112, second paragraph, for indefiniteness is respectfully traversed in view of the above amendments and the following remarks. Concerning claims 52 and 72, applicants submit that the recited species in the Markush group are each narrower than the generic term "pathogen" recited in claims 41 and 61. Hence, the dependent claims further limit their respective base claims; claims 52 and 72 are therefore proper. For these reasons, the rejection of claims 42-48, 52, 53, 59, 61-74, 76, and 79 should be withdrawn.

The rejection of claims 41-54 and 58-79 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,850,015 to Bauer et al. ("Bauer") is respectfully traversed.

Bauer teaches the hypersensitive response elicitor $HrpN_{Ech}$ of *Erwinia chrysanthemi* and its encoding nucleic acid. Bauer also teaches the preparation of transgenic plants that are pathogen resistant by using a DNA construct that includes the $hrpN_{Ech}$ nucleic acid and a pathogen-inducible promoter.

Claim 41 presently recites a method of imparting pathogen resistance to plants that includes, *inter alia*, the step of "providing a transgenic plant seed transformed with a transgene comprising a DNA molecule encoding a hypersensitive response elicitor polypeptide or protein from a bacterial plant pathogen and a promoter that is not pathogen-inducible. . . ." Claim 58 recites a plant produced according to the process of claim 41, and claims 59-60 recite a transgenic plant seed and a plant propagule, respectively, from a plant produced according to the process of claim 41.

Claim 61 presently recites a method of imparting pathogen resistance to plants that includes the step of "transforming a plant with a transgene comprising a DNA molecule encoding a hypersensitive response elicitor polypeptide or protein from a bacterial plant pathogen and a promoter that is not pathogen-inducible. . . ."

Claim 75 recites a transgenic plant produced by the process of "transforming a plant with a transgene comprising a DNA molecule encoding a hypersensitive response elicitor polypeptide or protein from a bacterial plant pathogen and a promoter that is not pathogen-inducible. . . ." Claims 76 and 77 recite a transgenic plant seed and plant propagule, respectively, from a plant according to claim 75.

To anticipate a claimed invention, a single reference must teach each and every limitation of the claimed invention. *Hybritech v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379, 231 USPQ 81, 90 (Fed. Cir. 1986). Bauer fails to teach or suggest each and every limitation of the presently claimed invention, because Bauer explicitly teaches the use of a pathogen-inducible promoter. In contrast, the presently claimed invention of claims 41, 61, and 75, as well as claims dependent thereon, recites a promoter that is not pathogen-inducible.

For this reason, the rejection of claims 41-54 and 58-79 as anticipated by Bauer is improper and should be withdrawn.

The rejection of claims 41-54 and 58-79 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,174,717 to Beer et al. ("Beer") is respectfully traversed.

Beer teaches the hypersensitive response elicitor $HrpN_{Ea}$ of *Erwinia amylovora* and its encoding nucleic acid. Beer also teaches preparation of DNA constructs including the $hrpN_{Ea}$ gene and various inducible promoters, which can be used to prepare transgenic plants. In particular, Beer suggests using pathogen-inducible promoters to prepare pathogen-resistant plants.

Beer fails to teach or suggest each and every limitation of the presently claimed invention, because Beer explicitly teaches the use of a pathogen-inducible promoter. In contrast, the presently claimed invention of claims 41, 61, and 75, as well as claims dependent thereon, recites a promoter that is not pathogen-inducible.

For this reason, the rejection of claims 41-54 and 58-79 as anticipated by Beer is improper and should be withdrawn.

The rejection of claims 41-54 and 58-77 under the judicially-created doctrine of obviousness-type double patenting over claim 16 of Bauer is respectfully traversed.

The teachings of Bauer are set forth above.

Claim 16 of Bauer depends from claim 15, which depends from claim 13, which depends from independent claim 1. Claims 1, 13, 15, and 16 are set forth below:

> 1. An isolated DNA molecule encoding a protein or polypeptide corresponding to a protein or polypeptide in Erwinia chrysanthemi which elicits a hypersensitive response in plants, wherein said isolated DNA molecule has the nucleotide sequence of SEQ. ID. No. 6.
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> * * *
>
> 13. A method of imparting pathogen resistance to plants comprising:
> transforming a plant with the DNA molecule of claim 1 with a pathogen inducible promoter in a plant transformation vector.
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> * * *
>
> 15. A method according to claim 13, wherein the plant is selected from the group consisting of dicots and monocots.
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> * * *
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> 16. A method according to claim 15, wherein the plant is selected from the group consisting of rice, wheat, barley, rye, corn, potato, sweet potato, bean, pea, chicory, lettuce, endive, cabbage, cauliflower, broccoli, turnip, radish, spinach, asparagus, onion, garlic, eggplant, pepper, celery, carrot, squash, pumpkin, zucchini, cucumber, apple, pear, quince, melon, plum, cherry, peach, nectarine, apricot, strawberry, grape, raspberry, blackberry, pineapple, avocado, papaya, mango, banana, soybean, tobacco, tomato, sorghum, and sugarcane.

Claim 16, dependent ultimately on claim 13, requires the presence of a pathogen-inducible promoter. The presently claimed invention recites, as noted above, the presence of a promoter that is not pathogen inducible. Thus, the subject matter of Bauer claim 16 is excluded from the scope of the claimed invention. Because the invention claimed in Bauer fails to teach or suggest the above-identified steps of claims 41, 61, and 75, the obviousness-type double patenting rejection of claims 41-54 and 58-79 is improper and should be withdrawn.

In view of the all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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